

Titel: Development of novel methodologies for immunogen preparation for the generation of diagnostic and therapeutic antibodies

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Area of interest:

Peptide- and glycopeptide synthesis, conjugation chemistry, immunogen preparation, immuno-chemistry

Aim:

Synthetic peptides that mimic specific epitopes of antigenic proteins have proven valuable for the development of new diagnostic or therapeutic systems of several human diseases. A major aspect of these approaches focuses on the induction of peptide specific antibodies that cross react with the native protein. To significantly enhance their potential to elicit a strong humoral immune response synthetic peptides usually have to be coupled to carrier proteins such as Keyhole limpet hemocyanin (KLH). In recent years a variety of conjugation methods have been developed for the efficient and selective preparation of such immunogens including the addition of sulfhydryl groups to maleimides or the use diethyl squarate as homobifunctional coupling reagent. While being very effective for rapid conjugate formation, these procedures often incorporate aromatic or other cyclic structural elements, which are potentially highly immunogenic themselves, and may suppress an antibody response towards the desired target antigen. The main focus of the proposed research project, therefore, involves the exploration and development of novel, immunologically neutral conjugation strategies for the preparation of tailor-made immunogens. In addition, the potential of specific T_H-cell peptide epitopes to serve as efficient carriers in synthetic immunogens will be investigated.

Methodological Approach:

The key elements of the proposed project include:

- All aspects of solid-phase peptide synthesis including the preparation of modified peptides such as glycopeptides or peptides incorporating labels, dyes or unnatural amino acids
- Development of a novel linker methodology for immunogen preparation, which may include the synthesis of modified amino acid building blocks
- Performing protein conjugations in buffer systems
- Exploring different proteins for their potential to serve as suitable carriers
- Identification and evaluation of suitable T_H-cell peptide epitopes and their incorporation into peptide immunogens
- The prepared immuno conjugates will be tested in the Antibody Development unit and the induced antibodies will be evaluated by ELISA and Biacore